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ALL-UNION CONFERENCE ON THE DIRECTED MODIFICATION AND SELECTION OF MICROORGANISMS, MOSCOW, NOVEMBER 1951

> A. S. Kriviskiy Inst Experimental Med Acad Med Sci USSR, Leningrad

Modification of the nature of bacteria is a very promising and entirely feasible task. Solution of problems with which microbiologists are confronted in connection with this task must lead to developments that will be of great advantage from the economic viewpoint. Thus, creation of new varieties of soil bacteria may be expected to raise the yields of grain crops and technical

Extensive application of Michurin's principles in microbiology proved to be fruitful. Microbiologists have learned how to change the nature of a microorganism in a predetermined direction by changing the conditions under which it lives. The principles of vegetative hybridization were found to be applicable to bacteria. By investigating the nature of bacteria and selecting conditions of existence corresponding to the bacteria's requirements, microbiologists now succeed in preserving newly acquired characteristics and, furthermore, are able to prevent the degeneration of new and useful varieties.

Problems in connection with this and related developments were discussed at an all-union conference held in Moscow in November 1951. This conference was organized by the Department of Biological Sciences, Academy of Sciences USSR, and the Institute of Microbiology, Academy of Sciences USSR. In the keynote address, entitled "Modifiability and Selection of Microorganisms," Professor A. A. Imshenetskiy, Institute of Microbiology, Academy of Sciences USSR, criticized foreign metaphysical theories of dissociation and cyclogeny, which explain modifications occurring in bacteria by cyclic changes proceeding along a closed circle. He also criticized the harmful US theory of mutationism. He further pointed out that bacteria can be modified with particular facility due to the high rate of their propagation and the close contact with their environment; in some cases, only a few reseedings are necessary to fix a new

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characteristic which is transmitted by heredity. As far as vegetative hybridization of microorganisms is concerned, Imshenetskiy noted that a number of new and valuable investigations have been carried out on this subject in the USSR in recent years. These investigations, in his opinion, prove the possibility of transformation of one species of bacteria into another. Imshenetskiy further said that to establish the fact that vegetative hybridization took place, one must make sure that specific assimilation by the modified species of plastid substances from the "mentor" species had actually occurred.

An interesting example of the directed modification of biochemical properties of bacteria was mentioned in a paper presented by G. M. Frenkel', Institute of Microbiology, Academy of Sciences Ukrainian SSR. She succeeded in modifying Clostridium Welchii (the causative factor of gas gangrene) in such a manner that the resulting strains lost all pathogenic properties. These tacilli normally produce a complex toxin consisting of several enzymes. The greatest toxicity among the substances produced by Clostridium Welchii must be ascribed to alphatoxin, which contains lecithinase. The harmless strains developed by Frenkel' have an immunizing action and can be used for preventing anaerobic wound infections (gas gangrene).

Considerable attention was paid at the conference to the method of vegetative hybridization. As mentioned above, this method, which is of universal significance in biology, proved to be applicable to microorganisms as well. It is true that we are as yet unable to join two bacterial cells into a single organism. However, in view of the fact that bacteria obtain nourishment by absorbing food through the whole surface of their bodies, it is easy to bring about assimilation by one species of plastid substances, metabolism products, and products of cell disintegration derived from another species. Earlier work by N. A. Krasilinikov, N. P. Gracheva, et al. demonstrated that, after plastid substances of a different species have been assimilated, the species which assimilated these substances change their characteristics in such a manner that a resemblance to the so-called "mentor" species supplying the plastid substances is acquired by them. Thus, vegetative hybridization in microbiology may serve as an effective method of modifying inheritable characteristics of microorganisms in a controlled manner.

In a paper presented by Professor V. D. Timakov, Institute of Epideriology and Microbiology imeni N. F. Gamaleya, the modification of B. coli under the "directing" influence of paratyphoid and typhoid bacilli was discussed. When white mice had been infected with a strain of paratyphoid bacilli obtained from B. coli, the same pathological changes as those brought about by the original paratyphoid culture were obtained, according to the author. After typhoid or paratyphoid bacilli had been cultivated on the dead bodies or products of deterioration of B. coli, the bacteria in question acquired the properties of B. coli. In the author's opinion, complete transformation of one species of bacteria into another occurs under the conditions described by him. The change takes place gradually, in the beginning, only a few B. coli change their properties, but after 20-25 reseedings, the culture acquires all the serological and biochemical properties which are characteristic of the "directing" or "mentor" culture. Furthermore, after a few more reseedings, the newly acquired characteristics become firmly established and are transmitted from generation to generation.

According to Timakov's data, in all experiments of this type and under all conditions pertaining to them, a second species of bacteria is formed which does not resemble either the "mentor" culture or the original culture that has been modified. This species resembles in almost all its properties Bact. faecalis alcaligenes, however. According to data obtained by Timakov's group, a similar type of bacteria appears when the culture is subjected to the action of sulfonamides, antibiotics, or other strongly active substances.

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In discussing directed modification of microorganisms by growing them on a medium containing dead bodies of bacteria of a "mentor" species and substances produced by this species, Timakov raised the question as to whether filter the forms of the "mentor" or "directing" species were not also present. He answered this question in the negative, stating that directed modification took place notwithstanding the fact that heating to a sufficiently high temperature to kill all filterable forms was applied.

Professor G. P. Kalina, chair of microbiology, Chernovitsy Medical Institute, discussed the possibility that B. coli may be modified into pathogenic forms by vegetative hybridization under natural conditions (e.g., in the intestine of a subject suffering from dysentery.) Kalina further stated that from the biochemical viewpoint, two cellular components may be considered as being of possible importance in conferring new properties to bacteria: (1) the carrier of the specific actigenic properties of the cell, the so-called glucidolipidoprotein complex; and (2) the cell nucleoproteid. Kalina's experiments showed that only introduction of nucleoproteids extracted from paratyphoid bacilli into the autritive medium brought about transformation of B. coli into a strain which was rapidly agglutinated at a high dilution (1: 1,600) under the action of specific antiparatyphoid serum. On the other hand, the complete antigen had no effect whatever, according to Kalina's data (this is contrary to results obtained by Timakov, according to whom the carrier of specific antigenic properties did contribute to the transformation of B. coli Kaliba assumes that the sucleograteids are identical with in his experiments' filterable forms of the "mentor" species.

Professor M. N. Meysel? Institute of Microbiology, Academy of Sciences USSR, discussed the effect of strongly acting factors on microorganisms. Although he stated that, generally speaking, useful and viable modifications cannot be expected to arise as a result of the action of strong poisons, antibiotics, intensive irradiation, etc., the method in question is still applicable for certain practical purposes. Thus, the action of potassium cyanide may damage the synchrome respiratory system of a microorganism, forcing it to overdevelop its flavin system to compensate the damage. Under the circumstances, the synthesis of vitamin by will be stimulated. In the same manner, the synthesis of an autibiotic can be stimulated or forms with a modified type of protein synthesis can be bred for use as protein fodder.

Professor N. P. Terusalimskiy, Institute of Microbiology, Academy of Sciences USSR, presented a paper devoted to the preservation of useful properties of micro-organisms, once these properties have been developed

Professor F. T. Gribbaum, Institute of Epidemiology and Microbiology, Gor'kiy, made a special report dealing with changes which pathogenic bacteria undergo as a result of exposure to the natural conditions under which they exist. In discussing various aspects of this subject, which is important from the epidemiological viewpoint, Gribbaum mentioned that in cases of infection with typhoid, the typhoid batilli are first found in the blood, but later enter the intestine. The bacilli eliminated from the intestine during the period of convalences, are modified to such an extent that they ian hardly be regarded as typhoid bacilli any longer. Investigations carried out by Gribbaum's collaborators, Z. I. Galunina and Ye. A. Sosina proved that the bacilli in question have been actually modified. The results obtained on bacilli isolated from patients could be confirmed in experiments carried out on white mice. When both normal mice and mice immunized against typhoid bacilli were infected with a virulent strain of typhoid, the immunized mice yielded both typical and atypical (modified) variations of typhoid bacilli.

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According to further results reported by Grinbaum, typhoid bacilli also undergo extensive modifications when they are forced to live in water. In becoming adapted to this medium, they change their heredity, becoming nonvirulent, and acquiring different antigenic and biochemical properties. Occasionally, such forms could be changed into typical typhoid bacilli. It is worth noting that exactly the same atypical bacilli have been isolated from the water of wells that were known to be sources of typhoid infection.

In a report dealing with the problem of species formation, Professor S. B. Muromtsev, acting member, Academy of Agricultural Sciences imeni V. I. Lenin, cited numerous examples of the formation of microorganism species, viz., transformations in the intestinal typhoid group, formation of the causative factor of pseudotuberculosis of rodents from B. pestis. transition of hemolytic streptococci into green (zeleneyushchiye) streptococci Str. viridans?, etc.

In connection with the work outlined at the conference, differentiation of species of microorganisms is of considerable importance. Work conducted by members of the Institute of Microbiology, Academy of Sciences USSR, in the course of which it was established that specific antagonism exists between different species of bacteria or actinomycetes, but is not exhibited between varieties or strains within the same species, is of interest from this viewnoint.

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